A COMPREHENSIVE REVIEW OF THE CORRELATION BETWEEN VITAMIN D LEVELS AND MULTIORGAN FUNCTION IN OBESE CHILDREN

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ABSTRAK
Obesitas pada anak-anak merupakan masalah kesehatan global yang semakin umum, terkait dengan komplikasi metabolik, kardiovaskular, dan inflamasi. Vitamin D memainkan peran penting dalam metabolisme glukosa dan lipid serta memiliki efek anti-inflamasi; namun, perannya pada anak-anak obesitas masih kurang dieksplorasi. Tujuan studi ini adalah untuk menganalisis hubungan antara status vitamin D dan hasil metabolik pada anak-anak obesitas berdasarkan uji klinis terkontrol acak (RCT). Ulasan literatur dilakukan menggunakan basis data PubMed, ScienceDirect, dan Cochrane Library untuk RCT yang diterbitkan antara tahun 2021 dan 2025. Kata kunci yang digunakan meliputi "Vitamin D," "1,25$(OH)_2D_3$," "Calcitriol," "Obesitas," "Anak," "Anak-anak," dan "Kehidupan Anak-anak." Studi yang memenuhi syarat adalah artikel teks lengkap berbahasa Inggris dengan desain RCT. Hasil studi ini melaporkan bahwa tujuh RCT dimasukkan. Anak-anak obesitas secara konsisten menunjukkan kadar vitamin D yang lebih rendah dibandingkan dengan anak-anak dengan berat badan normal. Kekurangan vitamin D dikaitkan dengan resistensi insulin melalui gangguan sinyal reseptor vitamin D (VDR), serta dislipidemia dan peningkatan penanda inflamasi. Suplementasi vitamin D dosis tinggi (≥ 2000 IU/hari atau dosis awal 50.000 IU) terbukti secara signifikan meningkatkan kadar serum 25(OH)D menjadi ≥ 40 ng/mL, memperbaiki profil lipid, dan mengurangi peradangan sistemik. Kesimpulan: Defisiensi vitamin D pada anak obesitas memperburuk disfungsi metabolik melalui resistensi insulin, kelainan lipid, dan peradangan kronis.

Kata kunci **:** anak-anak, kalsiferol, kalsitriol, obesitas, vitamin D, 1,25$(OH)_2D_3$

ABSTRACT
Childhood obesity is an increasingly prevalent global health problem, associated with metabolic, cardiovascular, and inflammatory complications. Vitamin D plays an important role in glucose, lipid metabolism and has anti-inflammatory effects; however, its role in obese children remains underexplored. The aim of this study is to examine the relationship between vitamin D status and metabolic outcomes in obese children based on randomized controlled trials (RCTs). A literature review was conducted using the PubMed, ScienceDirect, and Cochrane Library databases for RCTs published between 2021 and 2025. Search terms included "Vitamin D," "1,25$(OH)_2D_3$," "Calcitriol," "Obesity," "Child," "Children," and "Childhood." Eligible studies were full-text, English-language articles with an RCT design. The results of this study reported that seven RCTs were included. Obese children consistently showed lower vitamin D levels compared with normal-weight children. Deficiency was associated with insulin resistance through impaired vitamin D receptor (VDR) signaling, as well as dyslipidemia and increased inflammatory markers. High-dose vitamin D supplementation (≥ 2000 IU/day or a 50,000 IU loading dose) was shown to significantly increase serum 25(OH)D levels to ≥ 40 ng/mL, improve lipid profiles, and reduce systemic inflammation. The conclusion vitamin D deficiency in obese children exacerbates metabolic dysfunction through insulin resistance, lipid abnormalities, and chronic inflammation. Supplementation can improve vitamin D status and potentially provide metabolic benefits, although long-term outcomes still require further research.

Keywords ***:*** *children, calciferol, calcitriol, obesity, vitamin D, 1,25$(OH)_2D_3$*

INTRODUCTION

Childhood obesity is an escalating global public health concern, including in Indonesia (Jebeile et al., 2022). World Health Organization (WHO) defines childhood obesity as a body mass index (BMI) ≥ 2 standard deviations above the median for age and sex.(Jebeile et al., 2022) According to the World Obesity Federation, an estimated 206 million children will be obese by 2025, increasing to 254 million by 2030 among those aged 5–19 years.(Zhang et al., 2024) It is projected that by 2030, more than one million obese children will be found in at least 42 countries, with China ranking highest, followed by India, the United States, Indonesia, and Brazil. Obesity is a chronic, multifactorial metabolic condition characterized by excessive adipose tissue accumulation. In obese individuals, vitamin D is sequestered in adipose tissue, leading to decreased circulating levels and impaired metabolism in the liver and kidneys.(Lee, 2025) In children, the role of vitamin D extends beyond bone health, contributing to the prevention of metabolic complications, regulation of immune function, and maintenance of neuromuscular and cognitive integrity.(Wimalawansa, 2024a)

Vitamin D is an essential micronutrient obtained from ultraviolet B (UVB) exposure, dietary intake, and supplementation. Within the body, vitamin D undergoes complex metabolic processes to form its active metabolite, calcitriol, which functions as a hormone regulating calcium and phosphate homeostasis.(Wimalawansa, 2024a) Deficiency of vitamin D has been shown to contribute significantly to the progression of various pathological conditions and increase the risk of complications such as cardiovascular disease, infections, cancer, muscle weakness, impaired calcium absorption, rickets, and osteomalacia.(Wimalawansa, 2024a) In obese children, vitamin D deficiency further worsens metabolic dysregulation, including insulin resistance, cardiovascular risk, and chronic low-grade inflammation.(Deruyter et al., 2023) Global reports indicate that the prevalence of vitamin D deficiency among children ranges from 40% to 75%, affecting populations in both developed and developing countries.(7) A regional study in Bahrain reported that 92.1% of children and adolescents had deficiency (<20 ng/mL), with the highest prevalence among overweight/obese individuals.(Al-Ajlan et al., 2023) In Indonesia, hypovitaminosis D has been reported in 33% of children, with a higher proportion in girls than boys.(Octavius et al., 2023).

The magnitude of this problem underscores the urgent need for preventive and interventional strategies, particularly in countries predicted to face the highest burden of childhood obesity. Obesity is influenced not only by caloric imbalance but also by genetic susceptibility, endocrine regulation, epigenetic alterations, environmental exposures, and lifestyle behaviors such as sedentary activity and unhealthy dietary patterns(Almasri et al., 2024). The sequestration of vitamin D within adipose tissue represents a central mechanism for reduced bioavailability in obese individuals, compounded by impaired hepatic and renal hydroxylation processes. Furthermore, vitamin D is increasingly regarded as a pleiotropic hormone that impacts multiple organ systems, playing roles in immune modulation, insulin sensitivity, neuromuscular function, and cognitive development during childhood growth. Consequently, deficiency of vitamin D has broad systemic consequences, including cardiometabolic disturbances, enhanced risk of type 2 diabetes, and chronic inflammation driven by cytokines such as IL-6 and TNF-α (Marazziti et al., 2021).

Vitamin D deficiency has been documented in diverse populations, emphasizing its global relevance rather than being confined to specific regions. Sociocultural determinants, including limited sun exposure, traditional clothing practices, dietary inadequacies, and gender differences, contribute to variability in prevalence across countries, as observed in Indonesia where girls are more affected than boys. While vitamin D supplementation alone may not suffice as a treatment for obesity, optimizing serum vitamin D concentrations is clinically important to improve metabolic regulation, attenuate chronic inflammation, and preserve

multiorgan function. Integrating vitamin D repletion with lifestyle-based strategies offers a comprehensive approach to managing the health risks associated with childhood obesity. Given this background, the present literature review aims to comprehensively examine the correlation between vitamin D status and multiorgan function in obese children

METHODS

This study is a literature review using a systematic review design, conducted through searches in PubMed, ScienceDirect, and Cochrane Library databases with a publication range limited to 2021–2025 and restricted to English-language articles. The instrument applied in this research was the use of scientific databases with predefined Boolean operators and specific keywords to identify relevant studies. Data analysis was carried out through a screening process based on inclusion and exclusion criteria, which ultimately resulted in seven randomized controlled trials (RCTs) meeting the eligibility requirements. As this research is literature-based and does not involve direct human participants, ethical approval was not required.

RESULT

The literature search across PubMed, ScienceDirect, and the Cochrane Library yielded a total of 803 articles. After applying the inclusion and exclusion criteria, seven randomized controlled trials (RCTs) were eligible and included for review.

Table 1. Summarizes The Key Characteristics and Findings Of The Included Studies, Covering Study Design, Population, Intervention, Outcomes, and Main Conclusions Relevant To The Role Of Vitamin D Levels and Multiorgan Function in Obese Children

No	Author/ Year/ Country	Desain Studi	Populasi / sample size	Intervention	Target System	Outcome Measures	Main Findings	Conclusion
1	O'Sullivan B et al, 2024, USA.(O' Sullivan et al., 2024)	RCT (Open-label clinical trial)	112 obese children, 6–17 years	Loading dose 50,000 IU + 8,000 IU/day	Respiratory and vascular	Childhood Asthma Control Test (c-ACT) and Serum vitamin D concentration	78.6% reached ≥40 ng/mL; significant improvement vs 600 IU/day ($p<0.0001$)	Administration of the high-dose regimen was found to be a safe and effective approach for elevating serum 25(OH)D concentrations to ≥40 ng/mL
2	Lanf JE et al, 2023, USA.(Lang et al., 2023)	RCT, (Open-label pharmacokinetic study)	Obese children with asthma, 6–17 years	Loading 50,000 IU + 8,000 IU/day	Vascular	Serum vitamin D concentration	Majority achieved ≥40 ng/mL; faster attainment with high-dose regimen ($p<0.001$)	Obesity alters vitamin D clearance; loading dose + 8,000 IU/day effective

3	Morrissey C et al, 2022, France. (Morrissey et al., 2022)	RCT (Double Blind	26 obese adolescents, 12–17 yrs	4,000 IU/day	Vascular	ELISA, high-resolution vascular ultrasound	Negative correlation between BMI change and 25(OH)D (p=0.03)	Lifestyle program + vitamin D improved carotid IMT.
4	Sacheck JM et al, 2022, USA.(Sacheck et al., 2022)	RCT (Double-blind)	685 overweight/obese children, 8–15 yrs	600 IU, 1000 IU, 2000 IU/day	Cardiometabolic	LDL, HDL, triglycerides, total cholesterol	HDL remained high with 600–1000 IU; LDL and TC reduction sustained with 2000 IU (p=0.04, p<0.001)	Vitamin D improved lipid profile, most effective at 2000 IU/day
5	Dari Cosmi V et al, 2022, Italy.(De Cosmi et al., 2022)	RCT (Double Blind)	108 obese children, 6–14 yrs	1200 IU/day + 500 mg DHA and 1200 IU + wheat germ oil	Metabolic	Anthropometrics, metabolic markers	Both groups: ↓ fat mass percentage, improved BMI (p=0.030); ↓ TNF-α (p=0.048)	Vitamin D+DHA not superior to vitamin D+oil in improving vitamin D status
6	Alves A et al, 2021, Brazil.(Alves et al., 2021)	RCT, (Triple-masked)	44 children, 4–11 yrs, hypertriglyceridemia	1000 IU/day ×12 weeks	Cardiometabolic	Lipid profile	↓ total cholesterol, LDL, non-HDL (p=0.001)	Vitamin D improved lipid profile without altering body composition.
7	Vinet A et al, 2021, France.(Vinet et al., 2021)	RCT (Double-Blind)	26 obese adolescents, 12–17 yrs	4000 IU/day + lifestyle program	Vascular	High-resolution ultrasound (brachial artery)	Baseline deficient subgroup: 25(OH)D positively correlated with ↑ skin blood perfusion (p=0.002)	Vitamin D + lifestyle reduced microvascular dysfunction, not macrovascular

The table summarizes seven randomized controlled trials (RCTs) evaluating the effects of vitamin D supplementation in obese children and adolescents across different organ systems. Overall, various dosing regimens (ranging from 600 IU to 50,000 IU loading plus 8,000 IU/day) were shown to increase serum 25(OH)D levels and provide beneficial effects on respiratory, vascular, metabolic, and cardiometabolic functions. The findings indicate that both high and moderate doses of vitamin D can improve asthma control, enhance lipid profiles, reduce body fat, and lower inflammation and vascular dysfunction. However, the combination of vitamin D with other supplements such as DHA was not found to be superior to vitamin D alone. In conclusion, the table highlights that vitamin D supplementation has the potential to support multi-organ health in obese children, although its effectiveness may depend on dosage, baseline nutritional status, and concurrent lifestyle interventions.

DISCUSSION

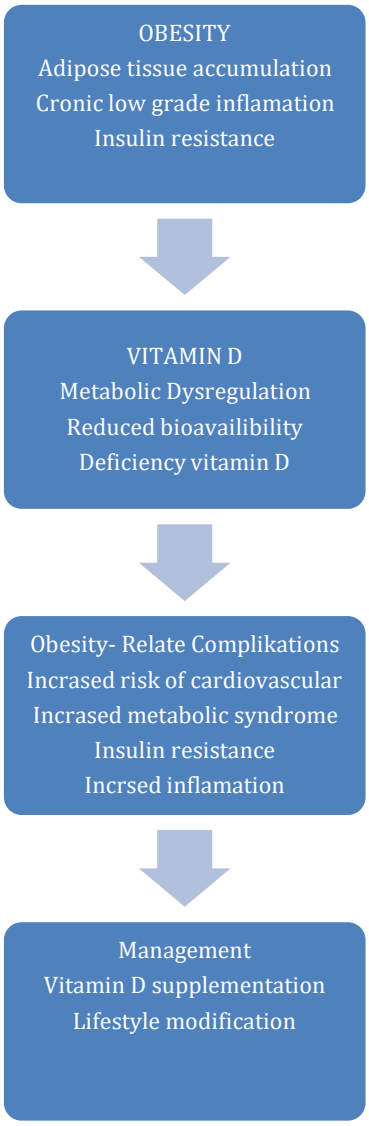

Figure 1. Pathophysiology of Vitamin D in Obese Children

Vitamin D is an essential micronutrient obtained through cutaneous synthesis and dietary intake. Following absorption, it undergoes the first hydroxylation in the liver to form calcifediol, and a second hydroxylation in the kidney to generate its active metabolite, calcitriol. Calcitriol binds to vitamin D receptors (VDRs) expressed in multiple tissues, including the pancreas, adipose tissue, skeletal muscle, and vascular endothelium (Wimalawansa, 2024a). Vitamin D plays a critical role in glucose metabolism within adipose and muscle tissues by enhancing the expression of insulin receptors, facilitating glucose uptake through the glucose transporter GLUT4, and activating peroxisome proliferator–activated receptor alpha (PPAR-α).(4) Beyond its classical functions, vitamin D exerts non-classical effects through VDR or retinoid X receptor (VDR/RXR) modulation in the liver, kidney, and adipose tissue. This interaction with vitamin D response elements (VDREs) regulates the transcription of thousands of genes involved in metabolism, inflammation, adipogenesis, and the homeostasis of glucose and lipid balance (Wimalawansa, 2024a) (Bennour et al., 2022).

In children with obesity, vitamin D deficiency is associated with an increased risk of insulin resistance, accompanied by elevated blood glucose levels, which contribute to the early development of metabolic syndrome (Lee, 2025). Vitamin D deficiency is more prevalent

among obese children, with a reported prevalence of up to 50%, and obesity increases the risk of deficiency by approximately 41% compared to children with normal body weight. This condition is largely attributed to the sequestration of vitamin D within adipose tissue, which reduces its bioavailability and consequently lowers circulating serum levels.(De Cosmi et al., 2022) Vitamin D also plays a role in activating the peroxisome proliferator-activated receptor gamma (PPAR-γ) signaling pathway, which regulates hepatic lipid metabolism and exerts anti-inflammatory effects by reducing proinflammatory cytokines such as IL-6 and TNF-α, both of which are key mediators of chronic inflammation in obesity.(13) In addition, vitamin D suppresses the overproduction of IL-6 and TNF-α, which, when excessive, may exacerbate dyslipidemia by promoting lipolysis and impairing hepatic function. A 2022 meta-analysis reported that high-dose vitamin D supplementation (≥ 4000 IU/day) improved insulin resistance, reduced C-reactive protein (CRP) levels, and increased HDL cholesterol, although the clinical effects on BMI, lipid profile, and other metabolic parameters remained inconsistent or minima.(Gou et al., 2023)(Sacheck et al., 2022).

Beyond metabolic and cardiovascular risks, obese children with asthma often exhibit elevated levels of IL-6, TNF-α, and leptin, while serum vitamin D (25[OH]D_3) concentrations are lower compared with children who have only one of these conditions. Vitamin D exerts anti-inflammatory effects by downregulating IL-6 expression and modulating the Th1/Th2 balance, which may provide therapeutic benefits in the asthma–obesity phenotype characterized by T2-low inflammation.(Jiang et al., 2025). Vitamin D metabolism, tissue actions, and mechanistic links to metabolism — In humans, cholecalciferol (vitamin D_3) is synthesized cutaneously or obtained from the diet, converted in the liver to 25-hydroxyvitamin D (calcifediol) and then hydroxylated in the kidney to the active hormone calcitriol; calcitriol acts through the vitamin D receptor (VDR) and VDR–RXR complexes to regulate transcription of many genes involved in glucose and lipid metabolism, inflammation, and adipogenesis. This molecular signalling underpins reported effects on insulin receptor expression, GLUT4-mediated glucose uptake, and PPAR pathways in adipose and muscle tissue. Recent physiology and mechanistic reviews summarize these genomic and non-genomic pathways and their potential to influence systemic metabolic homeostasis (Wimalawansa, 2024b).

The observed correlation between vitamin D levels and obesity in children underscores the importance of vitamin D screening in high-risk pediatric populations. Although vitamin D supplementation has not been proven effective as a stand-alone therapy for weight reduction, its role in improving metabolic and inflammatory profiles remains clinically relevant.

CONCLUSION

Obese children exhibit lower vitamin D levels due to altered fat distribution affecting its bioavailability. Vitamin D supplementation can improve serum concentrations and provide metabolic benefits, although its effectiveness varies according to dose and duration. Screening for vitamin D deficiency in obese children is essential as part of a comprehensive management approach, even though vitamin D alone has not been proven effective as a standalone therapy for weight reduction.

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